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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/593,823	11/21/2006	Marisa E.E. Jaconi	2507-1089	5480

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EXAMINER	
GAMETT, DANIEL C	
ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/593,823	JACONI ET AL.	
	Examiner	Art Unit	
	DANIEL C. GAMETT	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of Group I, claim(s) 22-37, drawn to a composition comprising a biodegradable gel-based matrix, at least one active agent, and stem cells able to differentiate into cardiac tissue, a method of making and using said composition in the reply filed on 05/04/2009 is acknowledged.

2. The amendments of 05/04/2009 have been entered in full. Claims 1-21 and 38 are cancelled. Claims 22-37 are under examination.

Priority

3. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows: Provisional Application No. 60/555815 does not provide support for a matrix made of proteoglycans or polysaccharides as recited in claim 23, cytokines of the IL-6 family as recited in claims 29 and 30, and beta-blockers and thymosin β4, as recited in claim 31. Therefore, the subject matter of claims 23 and 29-31 has an effective filing date of March 23, 2005, the earliest date at which the instant disclosure was filed.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 22, 23, 26, and 32 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent No. 7410798, filed September 4, 2002. The '798 patent teaches a culture composition comprising pluripotent (embryonic) stem cells, a support structure, and one or more growth factors added to the medium (column 2, lines 34-36). The disclosed support structure is taught to be a gel made from extracellular matrix, including proteoglycans (paragraph bridging columns 9-10). Irrespective of any intended use, the '798 patent teaches a composition comprising a biodegradable gel-based matrix, at least one active agent and stem cells able to differentiate into cardiac tissue (as in claim 22), wherein the biodegradable gel-based matrix is made of fibrin or proteoglycans or polysaccharides (as in claim 23), wherein the active agents are growth factors (as in claim 26, and wherein the stem cells able to differentiate to cardiac tissue are embryonic stem cells (as in claim 36).

6. Claims 22-26, 28, and 32-36 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent No. 7214371, filed September 1, 2000. The '371 patent discloses methods of making and using tissue-engineered biografts. The methods include introducing mammalian cells into a three-dimensional porous polysaccharide matrix; growing said cells in said matrix in vitro until a tissue-engineered biograft is formed; and transplanting the tissue-engineered biograft onto myocardial tissue (see Abstract). A tissue-engineered cardiac biograft is constructed from mammalian cells that are selected from the group consisting of fetal cardiac cells, neonatal cardiac cells, fibroblasts, smooth muscle cells, endothelial cells, skeletal myoblasts, mesenchymal stem cells and embryonic stem cells (column 2, lines 46-50). The matrix further comprises controlled-release polymeric microspheres capable of releasing soluble angiogenic growth factors in a controlled manner (see claim 1); this is exemplified by the release of VEGF from the composite scaffolds (FIG. 9, FIG. 14). The '371 patent, therefore, teaches compositions that are indistinguishable from those recited in the instant claims, as they comprise the same cells, the same matrix materials and the same additional factors. These disclosures expressly or inherently anticipate the compositions and method of instant claims 22-26, 28, and 32-35.

7. Claims 22-26, 28, and 32-34 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent No. 7192604. The '604 patent discloses implantable biodegradable devices comprising, in certain embodiments, a porous nonwoven matrix combined with hydrogels, such as alginates (polysaccharides)(column 7 lines 9-12). The matrix may be modified to contain biologically active factors, including growth factors such as VEGF (column 7, lines 24-47). The matrices can be seeded or cultured with appropriate cell types prior to implantation for the

targeted tissue. The cells may be bone marrow cells, stromal cells, stem cells, embryonic stem cells, pluripotent cells, monocytes, umbilical cord cells, mesenchymal stem cells, and myoblasts (column 7, lines 48-64). This disclosure includes many cell types which can differentiate into cardiac tissue recited in the instant claims. The '604 patent, therefore, teaches compositions that are indistinguishable from those recited in the instant claims, as they comprise the same cells, the same matrix materials and the same additional factors. The compositions disclosed in the '604 patent expressly or inherently anticipate the compositions of instant claims 22-26, 28, and 32-34.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 27, 29-31, and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 7214371 as applied to claims 22-26, 28, and 32-35 above, and further in view of US Patent No. 7192604, US Patent No. 7410798, US Patent Application Publication 20020061837 (Lough), US Patent Application Publication 20030235561 (Vandenburgh), U.S. Patent Application Publication 20040006018 (Baker), Bock-Marquette et al., 2004 Nov 25;Nature 432(7016):466-472 and US Patent Application Publication 20020168718 (Hubbell).

10. The teachings of US Patent Nos. 7214371, 7192604, 7410798 are set forth above. It is clear from the '371 patent alone that compositions comprising a biodegradable gel-based matrix,

cells able to differentiate to cardiac tissue, and additional bioactive factors, as well as methods of using such compositions to repair damaged heart tissue, were well known in the art at the time the instant application was filed. This conclusion is further supported by the '604 and '798 patents. Furthermore, one of skill in the art would recognize that the general method for preparing such compositions recited in instant claim 37 is implicit in the prior art. Thus, although the references do not specifically teach cultivating cells for up to 14 days in order to allow cell differentiation, as recited in claim 37 step (d), the presence of undifferentiated pluripotent or multipotent stem cells in the starting material would suggest to the skilled artisan that some period of time for differentiation prior to implantation would be desirable. US Patent No. 7410798 teaches methods for generating and purifying hES cell derived cells that have characteristic markers of cardiomyocytes and spontaneous periodic contractile activity (column 15, lines 42-50). US Patent No. 7192604 teaches the cells can be seeded on scaffolds and cultured for several days to allow for cell proliferation and matrix synthesis within the seeded scaffold prior to implantation (column 7, lines 48-64). Therefore, the skilled artisan would be motivated and expect success in maintaining the cell/matrix/factor composition in culture in order to achieve appropriate differentiation; the amount of time of culture would be determined by routine optimization.

11. Additional limitations not specifically taught in the above references, but recited in the instant claims are found in the prior art. Vandenburgh (US 20030235561) teaches a cardiac muscle construct comprising myocytes in which the myocytes are provided within a fibrin gel, as recited in claim 22 [0157, 0160]. Hubbell (US 20020168718) teaches (throughout) a general protocol for incorporating peptide factors into fibrin gels wherein a sequence from α2-plasmin

inhibitor is added to the amino terminus of a peptide factor (recited in claim 27), which enables covalent incorporation of the modified factor into fibrin gels by means of the transglutaminase activity of Factor XIII. VEGF (recited in claim 28) linked to fibrin was shown to be biologically active (Example 5); factors can be released as the fibrin is degraded. Lough (US 20020061837) teaches compositions and methods for the induction of cardiogenesis; the compositions may comprise, among other factors, epidermal growth factor (EGF), transforming growth factor (TGF-β), insulin-like growth factor (IGF) [0021], recited in claim 28. Baker (US 20040006018) teaches that leukemia inhibitory factor (LIF) has cardiotrophin activity in that both induce cardiac myocyte hypertrophy *in vitro* and both act similarly in numerous assays [523-530]; LIF and cardiotrophin are recited in instant claims 29 and 30. Bock-Marquette et al., 2004 Nov 25;Nature 432(7016):466-472 show that thymosin β4 can stimulate migration of cardiomyocytes and endothelial cells and promotes survival of cardiomyocytes. Treatment of adult mice with thymosin β4 (recited in claim 31) after coronary ligation resulted in enhanced early myocyte survival and improved cardiac function (see Abstract). Thus, the additional factors recited in claims 28-31 are individually known or expected to be beneficial for treating damaged heart tissue due to their effects on stem cells, endothelial cells, cardiomyocytes or precursor cells. It would therefore be obvious to use any of them in combination with stem cells in compositions such as those taught in US Patent No. 7214371.

12. The gel matrix materials, cell types, bioactive factors, and methods recited in the instant claims have been successfully used in various combinations for the same recited purposes. The instant claims, therefore, require only the combining of prior art elements according to known methods to yield predictable results. The Supreme Court reaffirmed principles based on its

precedent that "[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." KSR International Co. v. Teleflex Inc. (KSR), 550 U.S. 398 at, 82 USPQ2d at 1395.

Conclusion

13. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel C. Gamett, PhD., whose telephone number is (571)272-1853. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on 571 272 0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Daniel C Gamett/
Examiner, Art Unit 1647